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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,564	11/07/2000	Florian Kern	KREISLER1089	5234

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EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/600,564	KERN ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-27* is/are pending in the application.

4a) Of the above claim(s) *15-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-21 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on 3-31-2006 are acknowledged. Claims 1 and 16 have been amended. Claims 14-27 are pending. Claims 22-26 remain withdrawn from consideration. Claims 13-21 and 27 are currently under examination.

Claim Rejections Withdrawn

The rejection of claims 14 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "selection and proliferation accompanied by the specific elimination of particular T cells do not occur" is withdrawn in light of the amendment thereto. It is unclear what is meant by said term. To which "particular T cells" is Applicant referring? Moreover, it is unclear what is meant by the term "specific elimination" since said term is not explicitly defined in the specification. Finally, it is unclear whether the aforementioned limitation is meant to include all forms of T cell elimination (death) or merely those subsequent to selection and proliferation. If the later is the case, how are the different types of elimination differentiated from one another?

The rejection of claim 16 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "the protein fragment essentially in a state bound to MHC class I or class II molecules is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claims 14-21 and 27 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons of record. The claim(s) still contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

Applicant argues:

1. The skilled artisan is aware that proliferation typically occurs not before 24 hours of stimulating T cells.

2. The protein fragments of the instant invention do not differ significantly in regards of the time required to be taken up by the MHC.

3. T-cell proliferation is not expected until about 24 to 48 hours after activation.

4. A time sufficiently short to avoid proliferation and sufficiently long to allow peptide uptake in the MHC-binding groove would therefore be understood as a time between several hours after stimulation, the exact time being system dependent (i.e. culture conditions etc).

5. The literature available prior to the filing date gave sufficient guidance as to the time frame in which proliferation can be expected as it was basic knowledge to anyone skilled in the art and is disclosed in the instant specification as being 6 hours.

6. Peptide loading of antigen presenting cells occurs within 30 to 45 minutes.

Applicant's arguments have been fully considered and deemed non-persuasive.

Applicant's arguments are directed to the establishment of the period of time between the uptake of peptide (activation) and the onset of proliferation. The claims however are drawn to the

period of time from antigen uptake to the onset of selection and proliferation **accompanied by elimination of T cells** (specific elimination of particular T cells in claim 27). Moreover, Applicant provides support for the lack of direction given with regard to the time between antigen uptake and the onset of proliferation when he states that proliferation is known in the art to begin 24 to 48 hours after stimulation whereas the specification clearly specifies that this time can be 6 hours (see page 9 of Applicant's response).

As outlined previously, undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors include, but are not limited to:

1. The breadth of the claims,
2. The nature of the invention,
3. The state of the prior art,
4. The level of one of ordinary skill,
5. The level of predictability in the art,
6. The amount of direction provided by the inventor,
7. The existence of working examples, and
8. The quantity of experimentation needed to make and/or use the invention based on the content of the disclosure.

The instant claims are drawn to methods for identification of T-cell stimulating protein fragments comprising the following steps:

- detecting an amino acid sequence of an antigen;

- subdividing the amino acid sequence into fragments;
- synthesizing at least one protein fragment;
- incubating a suspension containing T-cells with the protein fragment;
- identifying an induced T-cell cytokine or activation of a marker by flow cytometry;
- assigning experimental runs in which T-cells have been stimulated and the stimulation has been recognized by a T-cell cytokine or an activation marker.

The aforementioned method also requires that the incubation time of the protein fragment(s) with cell suspension containing T cells be of a duration "**sufficiently long** so that the protein fragment or fragments are sufficiently taken up by the major histocompatibility antigen (MHC) molecules said taking up being sufficient when an unambiguous identification of stimulated T cells is possible" and "... **sufficiently short** so that selection and proliferation accompanied by the specific elimination of particular T cells do not occur". The specification is silent with regard to what incubation time for a given protein fragment. Moreover, the specification is silent as how one would determine if "particular T cells" have proliferated and elimination has occurred. Given that immunological (T cell) responses are antigen dependent, one would not be able to predict what amount of time would be sufficient for the protein fragment or fragments to be sufficiently taken up by the major histocompatibility antigen (MHC) molecules said taking up being sufficient when an unambiguous identification of stimulated T cells is possible and **sufficiently short** so that selection and proliferation accompanied by the specific elimination of particular T cells do not occur. Moreover, the specification provides no working examples that provide guidance in making such a prediction. Consequently, since the amount of experimentation required to determine if a given protein or protein fragment would the protein

fragment or fragments are sufficiently taken up by the major histocompatibility antigen (MHC) molecules said taking up being sufficient when an unambiguous identification of stimulated T cells is possible and **sufficiently short** so that selection and proliferation accompanied by the specific elimination of particular T cells do not occur would be undue, the specification is not enabling for the claimed method.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 27 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "selection and proliferation accompanied by the specific elimination of particular T cells do not occur" is maintained for reasons of record. Applicant has indicated that said claim was amended thus obviating the rejection. However, to date, no such amendment has been made of record. As outlined previously, it is unclear what is meant by said term. To which "particular T cells" is Applicant referring? Moreover, it is unclear what is meant by the term "specific elimination" since said term is not explicitly defined in the specification. Finally, it is unclear whether the aforementioned limitation is meant to include all forms of T cell elimination (death) or merely those subsequent to selection and proliferation. If the later is the case, how are the different types of elimination differentiated from one another?

New Grounds of Rejection

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended claim 14 to recite, "proliferation accompanied by the elimination of T cells do not occur." This phrase does not appear in the specification, or original claims as filed. Applicant does not point out specific basis for this limitation in the application, and none is apparent. The specification does not seem to provide support for the elimination of any or all T cell types by any given process. Therefore this limitation is new matter.

Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended the claim 16 to recite, "the suspension comprises **cells which present the protein fragment bound to MHC class I or class II molecules.**" This phrase does not appear in the specification, or original claims as filed. Applicant does not point out specific basis for this limitation in the application, and none is apparent. The specification does not seem to provide support for all types of antigen presenting cells. Therefore this limitation is new matter.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ROBERT ZEMAN
PATENT EXAMINER

June 6, 2006